

IN THE SPECIFICATION

Page 1, line 2 (after the title), insert the following new paragraph.

RELATED APPLICATIONS

This application is a 371 of PCT/EP00/06215, filed July 4, 2000, which in turn claims priority to British application Serial No. 9917290.0, filed July 22, 1999.

Page 2, line 27 (before Figure 1) insert the following new paragraph.

Brief Description of the Drawings

Page 3, second full paragraph, please amend as follows:

The layer (I) is preferably of a material that permits the device to follow the contours of the skin and be worn comfortably on areas of the skin such as joints of flexure. Examples of flexible polymers useful for the backing layer include polyethylene, polypropylene, polyesters and the like, which may be provided as films or laminates. A preferred flexible polymer is a laminate consisting of pigmented polyethylene aluminum vapour coated polyester and a medium density polyethylene or ethylene vinyl acetate heat seal layer available from 3M™ under the trade mark ~~scotchpak~~TM SCOTCHPAKTM1006 (fluorine-coated polyester film laminate).

Page 4, first full paragraph, please amend as follows:

Conveniently fatty acid ester enhancers include esters of carboxylic acids containing from C₈ to C₁₆ carbon atoms. Preferred are those esters derived from palmitic acid, steric acid or lauric acid.

Conveniently fatty acid esters for use in the invention include fatty acid esters polyhydroxy alcohols such as sorbitol, glycerol or propylenglycol. Particularly preferred are fatty acids esters include those derived from sorbitol and of those sorbitan palmitate ~~SpanTM40~~ (SPANTM 40) (~~SpanTM40~~) is particularly preferred.

Page 4, second full paragraph, please amend as follows:

Use of combinations of two or more of the skin permeation enhancer compounds may frequently result in superior results, such as greater transdermal absorption. Thus it has been found that a mixture of ethanol, N-methyl-2-pyrrolidone and sorbitan palmitate (SPANTM 40) (~~SpanTM40~~) is a preferred skin permeation enhancing mixture.

Page 4, third full paragraph, please amend as follows:

The amount of ethanol present is conveniently within the range 10 – 60% e.g. 30 – 40% by weight of the total reservoir solution. The amount of SPANTM 40 (~~SpanTM40~~) is conveniently within the range 0.5 – 6.0% e.g. 1 – 5% of the total reservoir solution. The amount of N-methyl-2-pyrrolidone present is conveniently within the range 20 – 70% e.g. 40 – 70% by weight of the total reservoir solution.

Page 4, fifth full paragraph, please amend as follows:

A particularly preferred reservoir solution of the invention contains 3 – 5% e.g. 4% of a calcium antagonist of the dihydropyridine type, such as lacidipine, 30 – 40% e.g. 36.5% of ethanol, 3 to 5% e.g. 3.5% of SPANTM 40 (~~SpanTM40~~), and 50 – 60% e.g. 56% of N-methyl-2-pyrrolidone by weight of the total solution.

Paragraph bridging pages 4 and 5, please amend as follows:

The membrane (3) to control the release of the calcium antagonist of the dihydropyridine type is a thin, flexible uniformly microporous, flat sheet membrane which

provides a constant rate of drug release independent of time or of the amount of the active ingredient that remains in the reservoir. A preferred membrane is a flat sheet membrane made from food grade polypropylene and polyethylene resins known under the Trade Mark CELGARD™ 2400 or CELGARD™ 2500, available from Hoechst Celanese. ~~Celgard™ 2400~~ CELGARD™ 2400 is the preferred membrane. Other suitable membranes include a microporous polyethylene membrane SOLUPOR™ Soluper™ or an EVA membrane e.g. CO TRAN™ Co-Tran™ (translucent flexible backing).

Page 5, third full paragraph, please amend as follows:

Particularly preferred are the amine resistant silicone based pressure sensitive adhesives such as BIO-PSA Q7-4301® (amine resistant silicone based pressure sensitive adhesive) available from the Dow Corning Corp.

Page 5, fifth full paragraph, please amend as follows:

Release liners are typically treated with silicone or fluorocarbons. A fluoro coated polyester film under the Trade Mark ~~scotchak™ 1022~~ SCOTCHPAK™ 1022 available from 3M is particularly preferred.

Page 6, last paragraph, please amend as follows:

The individual TTS can be sealed into an appropriate packaging material using standard methods in the art. A convenient packaging material for use comprises a laminate of paper, polymer (i.e. polyethylene) and aluminum film. An example of a suitable means to seal the individual TTS into the appropriate packaging material is a polyethylene polymer available from DuPont and known under Trade Mark ~~Surlyn™ 2400~~ SURLYN™ 2400.

Page 7, fourth paragraph, please amend as follows:

N-methyl pyrrolidone (1.12 g) and sorbitan palmitate (~~SpanTM 40~~) (SPANTM 40) (0.07 g) were added to ethanol (0.737 g) and the solution obtained was stirred for about 30 min. Lacidipine (80 mg) was then added under stirring to obtain a homogeneous solution.

Page 7, sixth paragraph, please amend as follows:

A solution of the silicone adhesive (4) [BIO-PSA Q7-4301: silicone resin, amine resistant, high tack 200 g/cm²] was coated onto the release liner (5) (~~scotHPAK®1022~~) (SCOTHPAK®1022). The control membrane (3) ~~Celgard® 2400~~ CELGARD® 2400 was then laminated to the dried adhesive layer. The backing layer (1) ~~scotHPAK® 1006~~ SCOTHPAK® 1006 was then secured to the control membrane with a heat seal (7) to form a sachet (8) having a drug reservoir (2) connected to an opening (6). The drug reservoir (2) is then filled with the solution comprising lacidipine and at least one skin permeation enhancer via the opening (6) which is then heat sealed.

Page 8, last paragraph, please amend as follows:

N-methyl pyrrolidone (1.12 g) and sorbitan palmitate ~~spanTM 40~~ SPANTM 40 (0.07 g) were added to ethanol (0.737 g) and the solution obtained was stirred for about 30 min. Nifedipine (82 mg) was then added under stirring to obtain a homogeneous solution.